REMARKS

Reconsideration of this application is requested in view of the amendments to the specification and claims and the remarks presented herein.

The claims remaining in the application are claims 1 to 8 and 29 to 32 which are the elected claims. The non-elected claims have been cancelled but Applicants reserve the right to file a divisional application directed thereto. It should be noted that claim 29 should be combined with the elected invention as set forth in the restriction requirement in the office action of August 26, 2003. This is even more so since claims 30 to 32 are dependent thereupon.

Applicants have provided a new Abstract of the Disclosure and the specification has been amended to delete the embedded hyperlink codes therein. The specification has also been amended to recite the address of the Depository and the date and name of the Depository are already in the specification.

Claims 1, 2 and 30 to 32 were rejected under 35 USC 101 because the Examiner was of the opinion that the claimed invention was not supported by a specific and substantial asserted utility or a well established utility. The Examiner states that the specification discloses the open reading frame of SEQ ID No: 2, gene CaNL256 from

Candida Albicans and that the application does not give any evidence or guidance concerning the activity of the gene or if that expression or lacking of expression associated with the essential functions of the fungus. The Examiner is of the opinion that the Applicant has not adequately described any specific activity for the gene encoded by the SEQ ID No: 2. Therefore, it is doubtful whether the nucleotide sequences can have any of Applicants' asserted utilities according to the Examiner.

Applicants respectfully traverse this ground of rejection since it is deemed that the specification complies with the 35 USC 101 utility requirement. Applicants have cloned the *C.Albicans* homolog of YNL256 and it is an identification of the clone DNA is described by a homology research in the description on page 30.

With respect to the Examiner's allegation that the level of homology between YNL256 and cNL256 based on his own BLAST search. Applicants submit that the results of the BLAST search as shown in the search enclosed by the Examiner have not been properly interpreted. First, the matched DNA sequence YNL256w shown in the Examiner's enclosed documents is longer than its own open reading frame by 414 base pairs (as evidenced by the SwissProt protein sequence). The Examiner is comparing a sequence containing untranslated elements with a shorter genomic sequence isolated by the Applicant.

The matched sequence being longer than the reference, it is thus artificially reducing the numerical result "QUERY Match". As a cursory example, the 414 base pair difference in the BLAST search would lower the match percentage by 414/2364 = 18%. In addition, it is indicated in line 15 of page 30 that the coding region of CaNL256 is shorter than that of its YNL256 homolog and this would artificially lower the overall match score. Finally, the Applicant has stated in lines 17 to 18 of page 30 that account must be taken of the translational variant in *C. Albicans.*

If the BLAST search was performed without taking these into account, then the overall match score will be artificially lowered. For example, it is noticed that on the search extract submitted by the Examiner, result 7 appears to be a match between the sequence in issue and other sequence corresponding to the same gene disclosed by the same Applicant in corresponding foreign patents. Interestingly, the overall match score of the sequence itself is only 16.6% with a 99% local similarity, probably due to the size differences. Thus, the proper measure of similarity is the best local similarity which in the Examiner's search, appears to be already 49.7% with YNL256. The artificially low number of 12% query match is to be disregarded as numerical artefact produced by differing sizes. There is no reason to doubt the accuracy of the homology search performed by the Applicant and which yields similar pertinent results to that of the Examiner.

With respect to the doubts raised by the Examiner about the accuracy of the determination of the function of the cloned gene based upon the proposition that the similarity with both the DHPS and HPPK domains is unlikely, Applicants submit two publications herewith, namely, Ogata et al, Science, Vol. 293, pages 2093-2098 and Mouillon et al, Biochem. J., Vol. 363, pages 313-319. The Examiner's attention is directed to column 2 of page 2096 of Ogata et al and the Abstract of the Mouillon et al references which show that both in the plant and the bacterial kingdom, there are enzymes that have both DHPS and HPPK functions within folate and folic acid pathways. It appears to be a feature of such enzymes and therefore, it is likely that CaNL256 has all of these activities and there is no reason to doubt the Applicants' results owing to the presence of these two domains.

Finally, the homology of 52% at the nucleotide level is high enough in addition to the matching of specific highly conserved domains for a function to be assigned. It is further submitted that for unicellular organism, the mutation rate being high, there is considerable genetic drift across DNA regions which do not code for specific catalytic domains. Thus, homology results across long regions are to be lower than that in other life forms as indicated in lines 20 to 25 of page 13.

The quoted articles on functions assigned by homology do not make definite technical statements but, rather, give opinions. The Attwood et al reference states that it

is unadvisable to make functional assignments merely on "some degree of similarity". All that this could indicate is that if a homology is too low, then it would be less reliable. Moreover, with respect to Brenner, this states that without laboratory experiments, it is not possible to "know for certain". An examination of the USPTO revised guidelines shows that what is required is a credible utility not an absolute scientific certainty.

Credible utility is defined in the utility guidelines (page 5) that "Where an Applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office personnel as being "wrong". Rather, Office personnel must determine if the assertion of utility is credible (i.e. whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided). As assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion." (emphasis added) Therefore, it is deemed that claims 1, 2 and 29 to 32 comply with 35 USC 101 and withdrawal of this ground of rejection is requested.

The elected claims were rejected under 35 USC 112, first paragraph, as not being based upon an enabling disclosure since, in the Examiner's opinion, the claims contain subject matter which is not described in the specification so as to reasonably convey to one skilled in the art that Applicant had possession of the claimed invention at the time of filing the application. The Examiner states that the claims are directed to polynucleotides

of SEQ ID No: 2, homologs and functional fragments thereof are genus claims that encompass a wide variety of molecules which are not sufficiently described in the specification.

Applicants respectfully traverse these grounds of rejection since it is deemed that the homologs and functional fragments thereof are within the reach of one skilled in the art. The description teaches that the gene claimed is the homolog of YNL256w as indicated in Example 1 on pages 29 and 30. Thus, its function is that of its homologs in *S.Cerevisia* and specifically has HPPK and DHPS activity as indicated on page 31. In addition, the specification makes it clear that this gene is selected because it is essential meaning that a deletion of it is lethal as indicated in lines 9 to 11 of page 6 which can be assessed easily. Thus, one skilled in the art is perfectly able to clone by routine means, homologs of SEQ ID No: 2 and to obtain fragments thereof and select a clone suitable for working the invention. The claimed sequences can thus be obtained by one skilled in the art and are enabled.

The written requirement of 35 USC 112 does not require that <u>all</u> possible embodiments be expressly described in terms of sequence or structure to show possession of the invention. The Examiner's attention is directed to two recent decisions, namely, Enzo Biochem v. Gen-Probe Inc., 296 F.3d 1316, and Moba v. Diamond Automation, 325 F. 3d, 1306. In the Enzo case, sequences which were not sequenced or disclosed were claimed in accordance with 35 USC 112 because they were obtainable by one

skilled in the art and thus, enabled. More specifically, the Moba case held "The language of 112 indicates that a patent will contain an adequate description if it provides enough information to enable a person skilled in the art to make and use the invention."

"Any disclosure that enables one to make and use the invention also, by definition, shows that the inventor was in possession of that full invention."

"After all, to enable is to show possession and to show possession is to enable."

Clearly judicial opinion is adverse to a rule in which all sequences must be disclosed to be validly claimed especially, when they are properly enabled and as Judge Rader pointed out in the Moba case, this is impractical. In summary, the Applicant has provided structural information in the form of sequence data and functional information which would enable one skilled in the art to determine if a claimed variant is suitable for the invention and therefore, the claims comply with 35 USC 112, first paragraph, and withdrawal of this ground of rejection is requested.

Claims 1, 2 and presumably, 29 to 32 were rejected under 35 USC 112, second paragraph, as being indefinite since, in the Examiner's opinion, there was a logical disconnect between claims 1 and 2 and claims 29 to 30. The Examiner states that claim 1 recites a product and claims 29 to 32 recite a product in the preamble but have method steps in the body of the claims referring to steps that are no where in claim 1. Therefore, the inconsistency requires correction.

Applicants respectfully traverse this ground of rejection since it is deemed that Applicants are entitled to claim the invention as they see fit and claims 1 and 2 are product claims and claims 29 to 32 are product by process claims. The latter are directed to a sequence that can be obtained by a defined process and such wording is expressly permitted by the Examination Guidelines, see 2173.05(p). Claims directed to product-by-process or produce and process claims and is in the U.S. P.T.O. written description guidelines, see page 40, example 10, cited as means of overcoming the written description issues for claims to DNA sequences. These claims are clear and are proper under the guidelines. Therefore, withdrawal of this ground of rejection is requested.

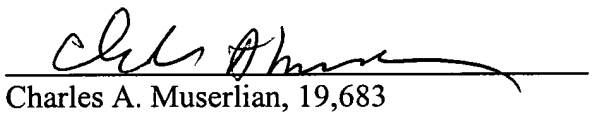
All of the elected claims were rejected under 35 USC 102 as being anticipated by Accession No. SCYNL256w which, according to the Examiner, is drawn to a sequence having homology and encoding fragments of SEQ ID No: 2. The Examiner deems that the prior art discloses a product which reasonably appears to be identical or with or only slightly different from Applicants' product claims.

Applicants respectfully this ground of rejection since the reference cited by the Examiner in no way anticipates or renders obvious Applicants' invention. SCYNL256w is the homolog of CaNL256 and *S.Cerevisia* and does not have the sequence of SEQ ID No: 2 as assumed by the Examiner. The homology being 50% according to Applicants and less according to the Examiner himself and most importantly, it is not a *C.Albicans* gene and it is clear that all of the claims are properly directed to *C.Albicans* genes and

there is no reason to consider that the sequences claimed by claims 29 to 32 which are functional genes from the *C.Albicans* could have the same sequence as the sequence of SCYNL256w. The CTG code difference in line 17 of page 30 and the size differs between the known homologs makes it extremely unlikely that there could be full sequence identity. However, the trilateral project 24.1 (Biotechnology Comparative Study) indicates that for the U.S.P.T.O., it is necessary to have sequence identity for anticipation to occur and for the purposes of novelty, the prior art is neither identical nor slightly different as the Examiner suggests and therefore, the Examiner has to show that the prior art discloses an identical sequence for an anticipation rejection. Therefore, withdrawal of this ground of rejection is requested.

In view of the amendments to the specification and claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
Muserlian, Lucas and Mercanti



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Enclosures